DATE: 12/20/2001

TIME: 08:55:03

OIPE

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      3 <110> APPLICANT: Wang, Tongwen
      5 <120> TITLE OF INVENTION: Composistions and Methods of modulating TGF-B Signaling
      7 <130> FILE REFERENCE: 17633/1082
C--> 9 <140> CURRENT APPLICATION NUMBER: US/09/927,738
     10 <141> CURRENT FILING DATE: 2001-08-10
     12 <150> PRIOR APPLICATION NUMBER: US 60/119786
     13 <151> PRIOR FILING DATE: 1999-02-11
     15 <150> PRIOR APPLICATION NUMBER: PCT/US00/03561
     16 <151> PRIOR FILING DATE: 2000-02-11
     18 <160> NUMBER OF SEQ ID NOS: 28
     20 <170> SOFTWARE: PatentIn version 3.1
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     23 <211> LENGTH: 277
     24 <212> TYPE: PRT
     25 <213> ORGANISM: Unknown
     27 <220> FEATURE:
     28 <223> OTHER INFORMATION: Isolated using yeast two hybrid system, Clone S1 + 27
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     36 Lys Tyr Thr Ala Phe Leu Tyr Asn Asp Gln Leu Ile Trp Ser Gly Leu
     40 Glu Gln Asp Asp Met Arg Ile Leu Tyr Lys Tyr Leu Thr Thr Ser Leu
     44 Phe Pro Arg His Ile Glu Pro Glu Leu Ala Gly Arg Asp Ser Pro Ile
     45
     48 Arg Ala Glu Met Pro Gly Asn Leu Gln His Tyr Gly Arg Phe Leu Thr
                            70
     52 Gly Pro Leu Asn Leu Asn Asp Pro Asp Ala Lys Cys Arg Phe Pro Lys
                                            90
                        85
     56 Ile Phe Val Asn Thr Asp Asp Thr Tyr Glu Glu Leu His Leu Ile Val
                                        105
                    100
     60 Tyr Lys Ala Met Ser Ala Ala Val Cys Phe Met Ile Asp Ala Ser Val
                                    120
               115
     64 His Pro Thr Leu Asp Phe Cys Arg Arg Leu Asp Ser Ile Val Gly Pro
                                                    140
                                135
     68 Gln Leu Thr Val Leu Ala Ser Asp Ile Cys Glu Gln Phe Asn Ile Asn
                                                155
                            150
     72 Lys Arg Met Ser Gly Ser Glu Lys Glu Pro Gln Phe Lys Phe Ile Tyr
                                                                175
                                            170
                        165
     76 Phe Asn His Met Asn Leu Ala Glu Lys Ser Thr Val His Met Arg Lys
                                                            190
                                        185
     80 Thr Pro Ser Val Ser Leu Thr Ser Val His Pro Asp Leu Met Lys Ile
                                    200
                                                        205
     84 Leu Gly Asp Ile Asn Ser Asp Phe Thr Arg Val Asp Glu Asp Glu Glu
                                215
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88 Ile Ile Val Lys Ala Met Ser Asp Tyr Trp Val Val Gly Lys Lys Ser

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/927,738

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/927,738 TIME: 08:55:03

DATE: 12/20/2001

Input Set : A:\initialseq.ST25.txt
Output Set: N:\CRF3\12192001\I927738.raw

235 89 225 92 Asp Arg Arg Glu Leu Tyr Val Ile Leu Asn Gln Lys Asn Ala Asn Leu 250 245 96 Ile Glu Val Asn Glu Val Lys Lys Leu Cys Ala Thr Gln Phe Asn Asn 260 265 100 Ile Phe Phe Leu Asp 275 101 104 <210> SEQ ID NO: 2 105 <211> LENGTH: 543 106 <212> TYPE: PRT 107 <213> ORGANISM: Unknown 109 <220> FEATURE: 110 <223> OTHER INFORMATION: Clone S1 + 28 protein 112 <400> SEQUENCE: 2 114 Phe Ala Val Asp Ala Lys Ala Leu Pro Gln Asn Lys Pro Arg Pro Leu 10 118 Thr Gln Glu Glu Ile Ala Gln Arg Arg Glu Arg Ala Arg Gln Arg His 2.5 122 Ala Glu Lys Leu Ala Ala Gln Gly Gln Ala Pro Leu Glu Pro Thr 40 126 Gln Asp Gly Ser Ala Ile Glu Thr Cys Pro Lys Gly Asp Glu Pro Arg 60 130 Gly Asp Glu Gln Gln Val Glu Ser Met Thr Pro Lys Pro Val Leu Gln 75 134 Glu Glu Asn Asn Gln Glu Ser Phe Ile Ala Phe Ala Arg Val Phe Ser 138 Gly Val Ala Arg Arg Gly Lys Lys Ile Phe Val Leu Gly Pro Lys Tyr 105 100 142 Ser Pro Leu Glu Phe Leu Arg Arg Val Pro Leu Cys Phe Ser Ala Pro 120 115 146 Pro Asp Gly Leu Pro Gln Val Pro His Met Ala Tyr Cys Ala Leu Glu 140 135 147 130 150 Asn Leu Tyr Leu Leu Met Gly Arg Glu Leu Glu Tyr Leu Glu Glu Val 150 155 151 145 154 Pro Pro Gly Asn Val Leu Gly Ile Gly Gly Leu Gln Asp Phe Val Leu 170 165 158 Lys Ser Ala Thr Leu Cys Ser Leu Pro Ser Cys Pro Pro Phe Ile Pro 185 180 162 Leu Asn Phe Glu Ala Thr Pro Ile Val Arg Val Ala Val Glu Pro Lys 200 166 His Pro Ser Glu Met Pro Gln Leu Val Lys Gly Met Lys Leu Leu Asn 215 170 Gln Ala Asp Pro Cys Val Gln Ile Leu Ile Gln Glu Thr Gly Glu His 171 225 230 235 174 Val Leu Val Thr Ala Gly Glu Val His Leu Gln Arg Cys Leu Asp Asp 250 175 178 Leu Lys Glu Arg Phe Ala Lys Ile His Ile Ser Val Ser Glu Pro Ile 179 265 182 Ile Pro Phe Arq Glu Thr Ile Thr Lys Pro Pro Lys Val Asp Met Val RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/927,738 TIME: 08:55:03

DATE: 12/20/2001

Input Set : A:\initialseq.ST25.txt
Output Set: N:\CRF3\12192001\I927738.raw

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|-----|------|--|-------|-------|-------------|------|-------------|-----|-----|-----|-----|-----|-----|-----|-------------|----------------|
| 186 | Asn | | Glu | Ile | Gly | Lys | | Gln | Lys | Val | Ala | | He | HIS | GIN | мет |
| 187 | | 290 | | | | | 295 | | _ | _ | | 300 | | _ | _ | |
| 190 | Lys | Glu | Asp | Gln | Ser | | Ile | Pro | Glu | Gly | | GIn | Va⊥ | Asp | Ser | |
| | 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| 194 | Gly | Leu | Ile | Thr | Ile | Thr | Thr | Pro | Asn | | Leu | Ala | Thr | Leu | | Val |
| 195 | | | | | 325 | | | | | 330 | | _ | | | 335 | |
| 198 | Arg | Ala | Met | Pro | Leu | Pro | Glu | G1u | | Thr | Gln | Ile | Leu | | Glu | Asn |
| 199 | | | | 340 | | | - | | 345 | | | | | 350 | | |
| 202 | Ser | Asp | Leu | Ile | Arg | Ser | Met | Glu | Gln | Leu | Thr | Ser | | Leu | Asn | Glu |
| 203 | | | 355 | | | | | 360 | | | | | 365 | | | |
| 206 | Gly | Glu | Asn | Thr | His | Met | Ile | His | Gln | Lys | Thr | Gln | Glu | Lys | Ile | \mathtt{Trp} |
| 207 | | 370 | | | | | 375 | | | | | 380 | | | | |
| 210 | Glu | Phe | Lys | Gly | Lys | Leu | Glu | Gln | His | Leu | Thr | Gly | Arg | Arg | ${\tt Trp}$ | Arg |
| | 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| 214 | Asn | Ile | Val | Asp | ${\tt Gln}$ | Ile | ${\tt Trp}$ | Ser | Phe | Gly | Pro | Arg | Lys | Cys | Gly | Pro |
| 215 | | | | | 405 | | | | | 410 | | | | | 415 | |
| 218 | Asn | Ile | Leu | Val | Asn | Lys | Ser | Glu | Asp | Phe | Gln | Asn | Ser | Val | Trp | Thr |
| 219 | | | | 420 | | | | | 425 | | | | | 430 | | |
| 222 | Gly | Pro | Ala | Asp | Lys | Ala | Ser | Lys | Glu | Ala | Ser | Arg | Tyr | Arg | Asp | Leu |
| 223 | - | | 435 | _ | _ | | | 440 | | | | | 445 | | | |
| 226 | Gly | Asn | Ser | Ile | Val | Ser | Gly | Phe | Gln | Leu | Ala | Thr | Leu | Ser | Gly | Pro |
| 227 | _ | 450 | | | | | 455 | | | | | 460 | | | | |
| 230 | Met | Cys | Glu | Glu | Pro | Leu | Met | G1y | Val | Cys | Phe | Val | Leu | Glu | Lys | \mathtt{Trp} |
| | 465 | - | | | | 470 | | _ | | _ | 475 | | | | | 480 |
| 234 | Asp | Leu | Ser | Lys | Phe | Glu | Glu | G1n | Gly | Ala | Ser | Asp | Leu | Ala | Lys | Glu |
| 235 | - | | | - | 485 | | | | | 490 | | | | | 495 | |
| 238 | Asp | Arq | Arg | Lys | Met | Lys | Pro | Val | Leu | Val | G1u | Met | Lys | Thr | Lys | Ser |
| 239 | _ | _ | _ | 500 | | - | | | 505 | | | | | 510 | | |
| | Tvr | Lvs | Met | Ala | Ala | Leu | Arg | Pro | Leu | Arg | Arg | Gly | His | His | Arg | Lys |
| 243 | - | - | 515 | | | | _ | 520 | | _ | | | 525 | | | |
| 246 | Glu | Asn | Leu | His | Ser | Leu | Thr | Ala | Met | Asp | Leu | Ser | Gln | Asp | Ser | |
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| 251 | <21 | l> LI | ENGT | H: 39 | 96 | | | | | | | | | | | |
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| 261 | | _1 _ | | | 5 | | | , | | 10 | - | | | | 15 | |
| 264 | Ara | Asp | Glv | Asp | Val | Val | Leu | Pro | | | Val | Val | Val | Lys | Gln | Glu |
| 265 | 9 | P | 1 | 20 | | | | | 25 | _ | | | | 30 | | |
| | Ara | Leu | Ser | | Glu | Val | Ala | Pro | | Ala | His | Arg | Arg | Pro | Asp | His |
| 269 | 9 | | 35 | | | | | 40 | _ | | | - | 45 | | _ | |
| | Ser | Glv | | Ser | Pro | Ser | Pro | | Thr | Ser | Glu | Pro | | Arq | Ser | Gly |
| 273 | | 50 | 1 | | | | 55 | • | | | | 60 | - | , | | • |
| | Hie | | Glv | Asn | Arg | Ala | | Glv | Val | Ser | Ara | | Pro | Pro | Lvs | Lys |
| 2,0 | | 7 | 1 | | 9 | | 9 | 1 | | | - 9 | | | | 4 | - |

RAW SEQUENCE LISTING DATE: 12/20/2001 PATENT APPLICATION: US/09/927,738 TIME: 08:55:03

Input Set : A:\initialseq.ST25.txt

Output Set: N:\CRF3\12192001\1927738.raw

277 65 70 75 280 Lys Asn Lys Ala Ser Gly Arg Arg Ser Lys Ser Pro Arg Ser Lys Arg 85 90 284 Asn Arg Ser Pro His His Ser Thr Val Lys Val Lys Gln Glu Arg Glu 100 105 288 Asp His Pro Arg Arg Gly Arg Glu Asp Arg Gln His Arg Glu Pro Ser 120 292 Glu Gln Glu His Arg Arg Ala Arg Asn Ser Asp Arg Asp Arg His Arg 135 296 Gly His Ser His Gln Arg Arg Thr Ser Asn Glu Arg Pro Gly Ser Gly 150 155 300 Gln Gly Gln Gly Arg Asp Arg Asp Thr Gln Asn Leu Gln Ala Gln Glu 170 304 Glu Glu Arg Glu Phe Tyr Asn Ala Arg Arg Arg Glu His Arg Gln Arg 180 185 308 Asn Asp Val Gly Gly Gly Ser Glu Ser Gln Glu Leu Val Pro Arg 312 Pro Gly Gly Asn Asn Lys Glu Lys Glu Val Pro Ala Lys Glu Lys Pro 215 220 316 Ser Phe Glu Leu Ser Gly Ala Leu Leu Glu Asp Thr Asn Thr Phe Arg 230 235 320 Gly Val Val Ile Lys Tyr Ser Glu Pro Pro Glu Ala Arg Ile Pro Lys 245 250 324 Lys Arg Trp Arg Leu Tyr Pro Phe Lys Asn Asp Glu Val Leu Pro Val 260 265 328 Met Tyr Ile His Arg Gln Ser Ala Tyr Leu Leu Gly Arg His Arg Arg 280 332 Ile Ala Asp Ile Pro Ile Asp His Pro Ser Cys Ser Lys Gln His Ala 295 336 Val Phe Gln Tyr Arg Leu Val Glu Tyr Thr Arg Ala Asp Gly Thr Val 310 315 340 Gly Arg Arg Val Lys Pro Tyr Ile Ile Asp Leu Gly Ser Gly Asn Gly 325 330 344 Thr Phe Leu Asn Asn Lys Arg Ile Glu Pro Gln Arg Tyr Tyr Glu Leu 340 345 348 Lys Glu Lys Asp Val Leu Lys Phe Gly Phe Ser Ser Arg Glu Tyr Val 355 360 352 Leu Leu His Glu Ser Ser Asp Thr Ser Glu Ile Asp Arg Lys Asp Asp 370 375 356 Glu Asp Glu Glu Glu Glu Glu Val Ser Asp Ser 357 385 390 360 <210> SEQ ID NO: 4 361 <211> LENGTH: 82 362 <212> TYPE: PRT 363 <213> ORGANISM: Unknown 365 <220> FEATURE: 366 <223> OTHER INFORMATION: Protein Sequence of NIPP-1 domain homologous to SNIP 1 368 <400> SEQUENCE: 4 370 Tyr Leu Phe Gly Arg Asn Pro Asp Leu Cys Asp Phe Thr Ile Asp His

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/927,738

DATE: 12/20/2001 TIME: 08:55:03

Input Set : A:\initialseq.ST25.txt
Output Set: N:\CRF3\12192001\1927738.raw

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371 1
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374 Gln Ser Cys Ser Arg Val His Ala Ala Leu Val Tyr His Lys His Leu
378 Lys Arg Val Phe Leu Ile Asp Leu Asn Ser Thr His Gly Thr Phe Leu
382 Gly His Ile Arg Leu Glu Pro His Lys Pro Gln Gln Ile Pro Ile Asp
386 Ser Thr Val Ser Phe Gly Ala Ser Thr Arg Ala Tyr Thr Leu Arg Glu
387 65
390 Lys Pro
394 <210> SEQ ID NO: 5
395 <211> LENGTH: 255
396 <212> TYPE: PRT
397 <213> ORGANISM: Unknown
399 <220> FEATURE:
400 <223> OTHER INFORMATION: Clone S1 + 19 Smad binding domain sequence
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404 Arg His Arg Gly His Ser His Gln Arg Arg Thr Ser Asn Glu Arg Pro
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412 Ala Gln Glu Glu Glu Arg Glu Phe Tyr Asn Ala Arg Arg Arg Glu His
416 Arg Gln Arg Asn Asp Val Gly Gly Gly Ser Glu Ser Gln Glu Leu
420 Val Pro Arg Pro Gly Gly Asn Asn Lys Glu Lys Glu Val Pro Ala Lys
424 Glu Lys Pro Ser Phe Glu Leu Ser Gly Ala Leu Leu Glu Asp Thr Asn
428 Thr Phe Arg Gly Val Val Ile Lys Tyr Ser Glu Pro Pro Glu Ala Arg
                                    105
432 Ile Pro Lys Lys Arg Trp Arg Leu Tyr Pro Phe Lys Asn Asp Glu Val
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436 Leu Pro Val Met Tyr Ile His Arg Gln Ser Ala Tyr Leu Leu Gly Arg
                            135
                                                140
440 His Arg Arg Ile Ala Asp Ile Pro Ile Asp His Pro Ser Cys Ser Lys
                        150
                                            155
444 Gln His Ala Val Phe Gln Tyr Arg Leu Val Glu Tyr Thr Arg Ala Asp
                    165
                                        170
                                                            175
448 Gly Thr Val Gly Arg Arg Val Lys Pro Tyr Ile Ile Asp Leu Gly Ser
                180
                                    185
452 Gly Asn Gly Thr Phe Leu Asn Asn Lys Arg Ile Glu Pro Gln Arg Tyr
           195
                                200
456 Tyr Glu Leu Lys Glu Lys Asp Val Leu Lys Phe Gly Phe Ser Ser Arg
                            215
                                                220
460 Glu Tyr Val Leu Leu His Glu Ser Ser Asp Thr Ser Glu Ile Asp Arg
                       230
                                            235
464 Lys Asp Asp Glu Asp Glu Glu Glu Glu Glu Val Ser Asp Ser
                    245
                                        250
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Use of n and/or Xaa has been detected in the Sequence Listing.

Review the Sequence Listing to incure a corresponding
Ciplanation is presented in the <220> to <223> fields of
cach sequence using n or Xaa.

Commence of the second second

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/927,738

DATE: 12/20/2001

TIME: 08:55:04

Input Set : A:\initialseq.ST25.txt

Output Set: N:\CRF3\12192001\I927738.raw

L:9 M:270 C: Current Application Number differs, Replaced Current Application Number

 $L:832 \text{ M}:341 \text{ W}: (46) "n" \text{ or "Xaa" used, for SEQ ID}\#:10 \\ L:931 \text{ M}:341 \text{ W}: (46) "n" \text{ or "Xaa" used, for SEQ ID}\#:11 \\ L:1240 \text{ M}:341 \text{ W}: (46) "n" \text{ or "Xaa" used, for SEQ ID}\#:16$